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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,076	11/08/1999	DENISA D. WAGNER	10861/011003	6116

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ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/02/2003

36

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/436076	Applicant(s) WAGNER
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 10/24/02 ; 3/18/03

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application. 40-41, 49-52, 54-60, 73-74

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 40-41, 49-52, 54-60, 73-74

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

PAPER NO. 34

DETAILED ACTION

1. To aid in correlating papers, applicant is required to employ the correct identifying information on communications sent to the USPTO. For example, the serial number of this application is **09**/436,076 and not 08/436,076.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission, filed on 3/18/03 (Paper No. 31),has been entered.

Claims 40-41, 49-52, 59-60 and 73-74 are pending.

Claims 40-41, 49-52, 59-60, 73-74 are being acted upon as the elected invention.

Claims 40-41, 49-52, 59-60, and 73-74, as they read on Groups I-III and V-XIII have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 1-39, 42-45, 46-48, 53-56, 57-58 and 61-72 have been canceled previously

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments in conjunction with the 1.131 declaration under 37 C.F.R. § 1.131, filed 3/18/03 (Paper Nos. 32/33).
The rejections of record can be found in the previous Office Actions (Paper Nos. 24/26/28).

3. Claims 40-41, 49-52, 59-60, 73-74 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 6,309,639) in view of Tedder et al. (U.S. Patent No. 5,834,425) and Coller et al. (U.S. Patent No. 5,976,532) for the reasons of record set forth in Paper No. 24.

Applicant's arguments in conjunction with the 1.131 declaration under 37 C.F.R. § 1.131, filed 3/18/03 (Paper Nos. 32/33), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the enclosed Declaration by the co-inventors demonstrates that the conception of the instant invention occurred as early as 1988 and that an actual reduction to practice occurred as early as 9/13/93. The time period between 11/16/92 and 9/13/93 was consumed by the development of a knockout mouse model for atherosclerosis and the testing of the mouse model to verify the inventive concept. It is noted that the conclusion of the results of the experiment were collected and analyzed on or about 5/6/94.

Applicant's rely on the statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." Applicant assert their conception of a functional relationship between E-selectin and P-selectin, and that P-selectin mediates the binding of platelets to macrophages (leukocytes implicated in atheroclerosis).

Applicant relied upon the preparing a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet. The results of this study demonstrate a reduction in the size of atherosclerotic lesions in P-selectin deficient mice.

Applicant assert that based upon these results that inhibitors of P-selectin/ligand binding and/or E-selectin/ligand binding would be useful for the treatment or inhibition of atherosclerosis, constituting an actual reduction to practice the claimed invention.

The evidence, submitted is insufficient to establish a reduction to practice of the invention in this country prior to the effective date of the prior art.

The 37 CFR 1.131 declaration must establish possession of either the whole invention claimed or something falling within the claim in the sense that the claims as a whole reads on it. In re Tanczyn 146 USPQ 298 (CCPA 1965). See MPEP 715.02.

Applicant has not overcome the prior art rejection by showing that the differences between the claimed invention and the showing under 37 CFR 1.131 would have been obvious to one of ordinary skill in the art, in view of applicant's 37 CFR 1.131 evidence, prior to the effective date of the references(s) or the activity.

The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the application possessed so much of the invention as is shown in the references. In re Schaub 190 USPQ 324 (CCPA 1976). See MPEP 715.03.

Applicant's evidence of conception and diligence does not address the critical elements of the instant claims which are drawn to a method of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

There is insufficient evidence the ordinary artisan would have taken applicant statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." to establish possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

Similarly there is insufficient evidence the ordinary artisan would have taken applicant preparation of a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet to establish possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

Further, it is noted that applicant's evidence relies upon experimental animals serves as model systems to selectively investigate different steps of the injury cascade providing specific insights into key mechanisms operating in diseases. While applicant's studies with a P-selectin knockout mouse may have provided insights into the role of P-selectin to atherosclerosis, there is insufficient evidence and correlation of establishing possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1, particularly given the absence of any disclosure of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1 in applicant's 131 Declaration and Exhibits.

Also, applicant has not provided objective evidence that applicant was in possession of PSGL-1 itself as well as its use as a therapeutic agent in treating restenosis prior to the disclosure of the prior art. Applicant's reliance on a generic concept of a possible role of P-selectin in atherosclerosis and subsequent findings in an experimental animal model does not support the use of PSGL-1 in treating restenosis.

Absent a clear support or facts are establishing applicant's assertions of conception and diligence (and reduction to practice or subsequent reduction to practice) before the prior art, applicant's arguments are not found persuasive and the rejection is maintained for the reasons of record (e.g., see Paper Nos. 24, 26 and 28).

Again, Cummings et al. teach the clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, by inhibiting platelet-leukocyte interactions with PSGL-1 and fragments thereof (see entire document, including Clinical Applications on columns 18-22 and Claims). Cummings et al. teach that the therapeutic use that reduce leukocyte adherence in ischemic myocardium can significantly enhance the therapy efficacy of thrombolytic agents (see column 18, paragraph 7).

Also, as pointed out previously, Coller et al. teach the art known vessel-corrective techniques at the time the invention was made in the treatment of cardiovascular disorders such as atherosclerosis and restenosis, including angioplasty, atherectomy and coronary bypass surgery (see Background of the Invention on column 1 and Utility of Platelet-specific Chimeric Immunoglobulin on columns 5-7). In teaching the use of an inhibitor of platelet aggregation and thrombus formation associated with such conditions, Coller et al. teach the art known use of combination therapy with other drugs such as thrombolytic agents and that the amounts administered before, along with or subsequent to treatment will depend on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made (see column 6, paragraphs 2-3).

In contrast to applicant's assertions of record, Cummings et al. and Coller et al. are drawn to the same or similar methods of inhibiting platelet-leukocyte / endothelial interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury as well as cardiovascular disorders such as atherosclerosis and restenosis, including angioplasty, atherectomy and coronary bypass surgery.

Given the art known practice of combination therapy, as taught by Cummings et al., Tedder et al. and Coller et al. as well as the art known practice of vessel-occlusive techniques to treat atherosclerosis and restenosis, as taught by Coller et al., one of ordinary skill in the art would have been motivated to administer the PSGL-1 and fragments thereof, as taught by Cummings et al. in various vessel-occlusive techniques given its properties of inhibiting platelet-leukocyte interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, as taught by Cummings et al. with an expectation of success.

Given the art known practice of modes of administrations and dosing depending on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made, as taught by Coller et al. In cardiovascular diseases, the claimed limitations were met or would have been obvious variants in meeting the needs of the patients in order to achieve a therapeutic effect depending on the symptom at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

4. No claim is allowed

5. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
May 30, 2003